

CLAIMS:

1. A composition for modulating bone regeneration, the composition comprising:

5 a matrix selected from the group consisting of glycolic acid, lactic acid, collagen, demineralized bone, or a combination thereof;

10 a first biologically active molecule comprising a fibronectin to facilitate osteoblast activity for promoting an increase in bone formation, the first biologically active molecule being attached to at least a portion of the matrix; and

15 a second biologically active molecule comprising a vitronectin selected for its ability to attract osteoclasts and produce an inhibiting effect on osteoclast activity to thereby promote a decrease in bone resorption, the second biologically active molecule being attached to at least a portion of the matrix substrate.

20 2. A composition as claimed in claim 1 wherein the fibronectin comprises an amino acid binding sequence that binds to the osteoblasts.

25 3. A composition as claimed in claim 2 wherein the amino acid binding sequence is selected from one or more of the group consisting of:

30 RGD-Type (Arg-Gly-Asp) and RGDS-Type (Arg-Gly-Asp-Ser), RGDC (Arg-Gly-Asp-Cys), RGDV (Arg-Gly-Asp-Val), RGES (Arg-Gly-Glu-Ser), GRGDS (Gly-Arg-Gly-Asp-Ser), GRADSP (Gly-Arg-Ala-Asp-Ser-Pro), KGDS (Lys-Gly-Asp-Ser), GRGDSP (Gly-Arg-Gly-Asp-Ser-Pro), GRGDTP (Gly-Arg-Gly-Asp-Thr-Pro), GRGES (Gly-Arg-Gly-Glu-Ser), GRGDSPC (Gly-Arg-Gly-Asp-Ser-Pro-Cys), GRGES (Gly-Arg-Gly-Glu-Ser-Pro), SDGR (Ser-Asp-Gly-Arg), YRGDS (Tyr-Arg-Gly-Asp-Ser), GQQHHLGGAKQAGDV

(Gly-Gln-Gln-His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val), GPR
(Gly-Pro-Arg);

GHK-Type (Gly-His-Lys);

YIGSR-Type (Tyr-Ile-Gly-Ser-Arg); PDSGR (Pro-Asp-Ser-Gly-Arg);

5 CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg); laminin or
laminin-fragment;

LCFR-Type (Leu-Cys-Phe-Arg);

EIL-Type, EILDV (Glu-Ile-Leu-Asp-Val), EILDVPST (Glu-Ile-Leu-
Asp-Val-Pro-Ser-Thr), EILEVPST (Glu-Ile-Leu-Glu-Val-Pro-Ser-Thr);

10 LDV-Type LDVPS (Leu-Asp-Val-Pro-Ser), LDV-NH₂ (Leu-Asp-Val-
NH₂);

synthetic peptides containing the RGD, RGDS, GHK, LCFR or
YIGSR sequence of amino acids;

15 osteonectin and SPARC (Secreted Protein Acidic and Rich in
Cysteine);

osteopontin;

collagens, Type I and Type II;

von Willebrand Factor;

bone sialoprotein;

20 thrombospondin;

osteocalcin;

cytomodulin;

bone morphogenetic proteins (BMPs);

tenascins;

25 fibrinolysis inhibiting factor;

growth factors, Platelet Derived Growth Factors (PDGF),
Insulin-Like Growth Factors (IGFs); and

antibodies to cell surface components, β -1; integrin antibody.

30 4. A composition as claimed in claim 1 wherein the vitronectin
comprises an amino acid binding sequence that binds to the
osteoclasts.

5. A composition as claimed in claim 4 wherein the amino acid binding sequence is selected from one or more of the group consisting of:

RGD-Type (Arg-Gly-Asp) and RGDS-Type (Arg-Gly-Asp-Ser), RGDC
(Arg-Gly-Asp-Cys), RGDV (Arg-Gly-Asp-Val), RGES (Arg-Gly-Glu-Ser),
GRGDS (Gly-Arg-Gly-Asp-Ser), GRADSP (Gly-Arg-Ala-Asp-Ser-Pro), KGDS
(Lys-Gly-Asp-Ser), GRGDSP (Gly-Arg-Gly-Asp-Ser-Pro), GRGDTP (Gly-
Arg-Gly-Asp-Thr-Pro), GRGES (Gly-Arg-Gly-Glu-Ser), GRGDSPC (Gly-
Arg-Gly-Asp-Ser-Pro-Cys), GRGESP (Gly-Arg-Gly-Glu-Ser-Pro), SDGR
(Ser-Asp-Gly-Arg), YRGDS (Tyr-Arg-Gly-Asp-Ser), GQQHHLGGAKQAGDV
(Gly-Gln-Gln-His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val), GPR
(Gly-Pro-Arg);

GHK-Type (Gly-His-Lys);

YIGSR-Type (Tyr-Ile-Gly-Ser-Arg); PDSGR (Pro-Asp-Ser-Gly-Arg);
CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg); laminin or
laminin-fragment;

LCFR-Type (Leu-Cys-Phe-Arg);

EIL-Type, EILDV (Glu-Ile-Leu-Asp-Val), EILDVPST (Glu-Ile-Leu-
Asp-Val-Pro-Ser-Thr), EILEVPST (Glu-Ile-Leu-Glu-Val-Pro-Ser-Thr);

LDV-Type LDVPS (Leu-Asp-Val-Pro-Ser), LDV-NH₂ (Leu-Asp-Val-
NH₂);

synthetic peptides containing the RGD, RGDS, GHK, LCFR or
YIGSR sequence of amino acids;

osteonectin and SPARC (Secreted Protein Acidic and Rich in
Cysteine);

osteopontin;

collagens, Type I and Type II;

von Willebrand Factor;

bone sialoprotein;

thrombospondin;

osteocalcin;

cytomodulin;

bone morphogenetic proteins (BMPs);

tenascins;
fibrinolysis inhibiting factor;
growth factors, Platelet Derived Growth Factors (PDGF),
Insulin-Like Growth Factors (IGFs); and
5 antibodies to cell surface components, β -1; integrin antibody.

6. A composition as claimed in claim 1 further comprising spacer
molecules between the matrix and the first and/or second
biologically active molecules.

7. A composition as claimed in claim 6 wherein the spacer
molecules are selected from homo-bifunctional or hetero-
bifunctional cross-linking agents.

8. A composition as claimed in claim 6 wherein the spacer
molecules comprise polymeric spacers.

9. A composition as claimed in claim 8 wherein the polymeric
spacers are selected from the group consisting of: polyethoxylates,
polyethylene glycol, polysorbitols, and combinations thereof.

10. A method of making a composition for modulating bone
regeneration comprising:

selecting a matrix from the group consisting of glycolic acid,
lactic acid, collagen, demineralized bone, or a combination
thereof;

attaching a first biologically active molecule comprising a
fibronectin to facilitate osteoblast activity for promoting an
increase in bone formation to at least a portion of the matrix; and

attaching a second biologically active molecule comprising a
vitronectin selected for its ability to attract osteoclasts and
produce an inhibiting effect on osteoclast activity to thereby

promote a decrease in bone resorption to at least a portion of the matrix substrate.

11. A composition for treating bone tissue comprising:

a matrix capable of forming a scaffold;

a first biologically active molecule comprising a fibronectin to facilitate osteoblast activity attached to at least a portion of the matrix; and

a second biologically active molecule comprising a vitronectin selected for its ability to attract osteoclasts attached to at least a portion of the matrix substrate..

12. A composition as claimed in claim 11 wherein the matrix forming a scaffold comprises a biodegradable or resorbable component, and the vitronectin is covalently anchored to the biodegradable component.

13. A composition as claimed in claim 11 wherein the matrix forming a scaffold comprises a biodegradable or resorbable component, and the fibronectin is covalently anchored to the biodegradable component.

14. A composition as claimed in claim 11 wherein the matrix is selected so that it has a differential disappearance rate which is a function of the polymerization thereof.

15. A composition as a claimed in claim 11 wherein the matrix is selected to control the time for degradation of the organic matrix.

16. A composition for inhibiting proteolysis of extracellular matrix in bone tissue, the composition comprising:

a biodegradable matrix forming a scaffold;

vitronectin attached to the matrix for release therefrom as the matrix degrades.

17. A composition as claimed in claim 16 wherein the matrix further comprises one or more from the group consisting of plasminogen activator inhibitor, metalloprotease inhibitor, protease inhibitors and combinations thereof, attached to the matrix.

18. A method of treating bone tissue comprising:
forming an inorganic matrix having a predetermined dissolution rate;

attaching vitronectin proteins to the matrix whereby vitronectin is released from the matrix in a controlled manner according to the rate of dissolution of the inorganic matrix.

19. A method as claimed in claim 18 wherein the vitronectin released from the matrix is bound to a plasminogen activator inhibitor, the plasminogen activator inhibitor being released from the vitronectin as the inorganic matrix dissolves to thereby reduce the production of proteolytic plasmin.